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(54) Title: POLYPEPTIDES AND NUCLEIC ACIDS ENCODING SAME

(57) Abstract: Disclosed herein are nucleic acid sequences that encode novel polypeptides. Also disclosed are polypeptides encoded by these nucleic acid sequences, and antibodies, which immunospecifically-bind to the polypeptide, as well as derivatives, variants, mutants, or fragments of the aforementioned polypeptide, polynucleotide, or antibody. The invention further discloses therapeutic, diagnostic and research methods for diagnosis, treatment, and prevention of disorders involving any one of these novel human nucleic acids and proteins.

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

polynucleotides" and the corresponding encoded polypeptides are referred to as "NOVX polypeptides" or "NOVX proteins." Unless indicated otherwise, "NOVX" is meant to refer to any of the novel sequences disclosed herein. Table A provides a summary of the NOVX nucleic acids and their encoded polypeptides.

TABLE A. Sequences and Corresponding SEQ ID Numbers

NOVX ASSIGNMENT	Internal Identification	SEQ ID NO (nucleic acid)	SEQ ID NO (polypeptide)	Homology
1	CG55758-01	1	2	SCUBE1-like
2a	CG55724-01	3	4	Adipocyte Complement Related Protein
2b	CG55724-03	5	6	Cq1 TNF-like
2c	CG55724-04	7	8	Cq1 TNF-like
2d	CG55724-06	9	10	Cq1 TNF-like
3	CG50345-01	11	12	β-Adrenergic Receptor Kinase-like
4	CG50301-01	13	14	TENM4-like
5a	CG55764-01	15	16	Out At First-like
5b	CG55764-02	17	18	Out At First-like
6a	CG55704-01	19	20	EphA6-ehk-like
6b	CG55704-03	21	22	EphA6-ehk-like
7	CG94323538	23	24	Glucose Transporter-like
8	CG95545-01	25	26	Type Ia Membrane Sushi-containing domain
9	CG95545-02	27	28	Type Ia Membrane Sushi-containing domain
10a	CG55746-01	29	30	Butyrophilin-like
10b	CG55746-05	31	32	Butyrophilin Precursor B7-DC
11	CG50329-01	33	34	Butyrophilin-like

NOVX nucleic acids and their encoded polypeptides are useful in a variety of applications and contexts. The various NOVX nucleic acids and polypeptides according to the invention are useful as novel members of the protein families according to the presence of domains and sequence relatedness to previously described proteins. Additionally, NOVX nucleic acids and polypeptides can also be used to identify proteins that are members of the family to which the NOVX polypeptides belong.

NOV1 is homologous to an EGF-Related SCUBE1-like family of proteins. Thus, the NOV1 nucleic acids, polypeptides, antibodies and related compounds according to the

section below. The disclosed NOV3 polypeptide has multiple hydrophilic regions, each of which can be used as an immunogen. In one embodiment, a contemplated NOV3 epitope is from about amino acids 20 to 70. In another embodiment, a contemplated NOV3 epitope is from about amino acids 95 to 115. In other specific embodiments, contemplated NOV3 epitopes are from about amino acids 120 to 190, 280 to 300, 305 to 375, 395 to 420, and 415 to 660.

NOV4

A disclosed NOV4 nucleic acid of 8354 nucleotides is set forth as SEQ ID NO:13 (designated CuraGen Acc. No. CG50301-01) encoding a TEN-M4-like protein is shown in Table 4A. An open reading frame was identified beginning with an ATG initiation codon at nucleotides 35-37 and ending with a TAG codon at nucleotides 8342-8344. Putative untranslated regions are indicated by underline.

Table 4A.
NOV4 Polynucleotide
SEQ ID NO:13

GTTTGTGGATGTGGAGGAGCGCGGGCCGGAGGCCATGGACGTGAAGGAGAGGAAGCCTTA	60
CCGCTCGCTGACCCGGCGCCGCGACGCCGAGCGCCGCTACACCAGCTCGTCCGCGGACAG	120
CGAGGAGGGCAAAGCCCCGCAGAATCTTACAGCTCCAGCGAGACCTGAAGGCCTACGA	180
CCAGGACGCCCGCCTAGCTATGGCAGCCGCGTCAAGGACATTGTGCCGCAGGAGGCCGA	240
GGAATTCTGCCGCACAGGTGCCAACTTCACCCTGCGGGAGCTGGGGCTGGAAGAAGTAAC	300
GCCCCTCAGGGACCCTGTACCGGACAGACATTGGCCTGCCCCAATGCGGCTACTCCAT	360
GGGGGCTGGCTCTGATGCCGACATGGAGCTGACACGGTGCTGTCCCCTAGCACCCCCT	420
GCGTCTGTGGGCCGGAGCACACGGTCAGGGCGCAGCTCCTCCCGCCTGTCCAGCCGGGCCAA	480
TTCCAATCTCACACTCACCGACACCGAGCATGAAAACTGAGACTGACTGATCATCCGGGCGG	540
CCTGCAGAACCACGCGGCGGCTCCGGACGCCGCCGCCGCCTCTCGCACGCCCACACCC	600
CAACCAGCACCACGCGGCCTCCATTACTCCCTGAACCGGGGCAACTTCACGCCGAGGAG	660
CAACCGCAGCCGCCGCCCCACGGACCACTCGCTCTCCGGAGAGCCCCCTGCCGGCGGCGC	720
CCAGGAGCCTGCCCACGCCCAGGAGAACTGGCTGCTCAACAGCAACATCCCCCTGGAGAC	780
CAGGAACCTAGGCAAGCAGCCATTCCTAGGGACATTGCAGGACAACCTCATTGAGATCGA	840
CATTCTCGGCGCCTCCGGCCATGATGGGGCTTACAGTGACGGGCACTTCCTTCTCAAGCC	900
TGGAGGCACCTCCCCGCTCTTCTGCACCCACATCACCAGGGTACCCACTGACGTCCAGCAC	960
AGTGTACTCTCCTCCGCCCCGACCGCTGCCCGCAGCACCTTCGCCCGGCCGGCCTTTAA	1020
CCTCAAGAAGCCCTCCAAGTACTGTAACTGGAAGTGCGCAGCCCTGAGCGCCATCGTCAT	1080
CTCAGCCACTCTGGTCATCCTGCTGGCATACTTTGTGGCCATGCACCTGTTTGGCCTAAA	1140
CTGCCACACCTGCAGCCGATGGAGGGGCAGATGTATGAGATCACGGAGGACACAGCCAGCAG	1200
TTGGCCTGTGCCAACCGACGTCTCCCTATACCCCTCAGGGGGCACTGGCTTAGAGACCC	1260
TGACAGGAAAGGCAAAGGAACCACAGAAGGAAAGCCCAGTAGTTTCTTCGAGAGGACAG	1320
TTTCATAGATTCTGGAGAAATTGATGTGGGAAGGCCAGCCTGCCACAAGATTCCTCCTGG	1380
CACTTTCTGGAGATCTCAAGTGTTCATAGACCTCCTGTGCATCTGAAATTCAATGTGTC	1440
TCTGGGAAAGGCAGCCCTGGTTGCATTATGGCAGAAAAGGCCTCCCTCCTTCACATAC	1500
ACAGTTTGACTTTGTTGTGAGCTGCTGGATGGCAGGAGGCTCCTAACCCAGGAGGCGCGGAG	1560
CCTGAGAGGGACCCCGCGCCAGTCTCGGGGAACTGTGCCCCCCTCCAGCCATGAGACAGG	1620
CTTCATCCAGTATTTGGATTCAGGAATCTGGCACTTGGCTTTTTACAATGACGGAAAGGA	1680
GTCAGAAGTGGTTTCCTTTCTCACCACTGCCATTGAGTCGGTGGATAACTGCCCCAGCAA	1740
CTGCTATGGCAATGGTGACTGCATCTCTGGGACCTGCCATCGTCTTCTGGGTTTCCTGGG	1800
CCCCGACTGTGGCAGAGCCTCCTGCCCGTGCTCTGAGCGGAAATGGCCAATACATGAA	1860
AGGCAGATGCTTGTGCCACAGTGGCTGGAAAGGCGCTGAGTGCGATGTGCCCACCAACCA	1920
GTGTATCGATGTGGCCTGCAGCAACCATGGCACCTGCATCACGGCACCTGCATCTGCAA	1980
CCCTGCTACAAGGGCGAGAGCTGTGAGGAAGTGGACTGCATGGACCCCACATGTTCAGG	2040
CCGGGGTGTCTGCGTGAGAGGCGAATGCCATTGCTTTGTGGGATGGGAGGCACCAACTG	2100
CGAGACCCCCAGGGCCACATGCTTAGACCAGTGTTCAGGCCACGGAACCTTCCTCCGGA	2160
CACCGGGCTTTGCAGCTGTGACCCAAGCTGGACTGGACACGACTGTTCTATCGAGATCTG	2220

TGCTGCCGACTGTGGTGGCCATGGCGTGTGCGTAGGGGGCACCTGCCGCTGCGAGGATGG	2280
CTGGATGGGGGCAGCCTGCGACCAGCGGGCCTGCCACCCGCGCTGTGCCGAGCATGGGAC	2340
CTGCCGCGACGGCAAGTGCGAGTGCAGCCCTGGCTGGAATGGCGAACACTGCACCATCGC	2400
TCACTATCTGGATAGGGTAGTTAAAGAGGGTTGCCCTGGGTTGTGCAATGGCAACGGCAG	2460
ATGTACCTTAGACCTGAATGGTTGGCACTGCGTCTGCCAGCTGGGCTGGAGAGGAGCTGG	2520
CTGTGACACTTCCATGGAGACTGCCTGCGGTGACAGCAAAGACAATGATGGAGATGGCCT	2580
GGTGGACTGCATGGACCCTGACTGCTGCCTCCAGCCCCTGTGCCATATCAACCCGCTGTG	2640
CCTTGGCTCCCCTAACCCTCTGGACATCATCCAGGAGACACAGGTCCCTGTGTCACAGCA	2700
GAACCTACACTCCTTCTATGACCGCATCAAGTTCCTCGTGGGCAGGGACAGCACGCACAT	2760
AATCCCCGGGGAGAACCCCTTTGATGGAGGGCATGCTTGTGTTATTCGTGGCCAAGTGAT	2820
GACATCAGATGGAACCCCCCTGGTTGGTGTGAACATCAGTTTTGTCAATAACCCTCTCTT	2880
TGGATATACAATCAGCAGGCAAGATGGCAGCTTTGACTTGGTGACAAATGGCGGCATCTC	2940
CATCATCCTGCGGTTCGAGCGGGCACCTTTCATCACACAGGAGCACACCCTGTGGCTGCC	3000
ATGGGATCGCTTCTTTGTCATGGAAACCATCATCATGAGACATGAGGAGAATGAGATTCC	3060
CAGCTGTGACCTGAGCAATTTTGCCCGCCCCAACCCAGTCGTCTCTCCATCCCCACTGAC	3120
GTCCTTCGCCAGCTCCTGTGCAGAGAAAGGCCCCATTGTGCCGGAAATTCAGGCTTTGCA	3180
GGAGGAAATCTCTATCTCTGGCTGCAAGATGAGGCTGAGCTACCTGAGCAGCCGGACCCC	3240
TGGCTACAAATCTGTCCTGAGGATCAGCCTCACCCACCCGACCATCCCCTTCAACCTCAT	3300
GAAGGTGCACCTCATGGTAGCGGTGGAGGGCCGCCTCTTCAGGAAGTGGTTCGCTGCAGC	3360
CCCAGACCTGTCCTATTATTTCATTTGGGACAAGACAGACGTCTACAACCAGAAGGTGTT	3420
TGGGCTTTCAGAAGCCTTTGTTTCCGTGGGTTATGAATATGAATCCTGCCCAGATCTAAT	3480
CCTGTGGGAAAAAAGAACAACAGTGCTGCAGGGCTATGAAATTGACGCGTCCAAGCTTGG	3540
AGGATGGAGCCTAGACAAACATCATGCCCTCAACATTCAAAGTGGTATCCTGCACAAAGG	3600
GAATGGGGAGAACCAGTTTGTGTCTCAGCAGCCTCCTGTCATTGGGAGCATCATGGGCAA	3660
TGGGCGCCGGAGAAGCATCTCCTGCCCCAGCTGCAACGGCCTTGCTGACGGCAACAAGCT	3720
CCTGGCCCCAGTGGCCCTCACCTGTGGCTCTGACGGGAGCCTCTATGTGGGTGATTTCAA	3780
CTACATTAGAAGGATCTTCCCCTCTGGAAATGTCACCAACATCCTAGAGCTGAGGAATAA	3840
AGATTTCAGACATAGTCACAGTCCAGCACACAAATACTACCTGGCCACAGACCCCATGAG	3900
TGGGGCCGTCTTCCTTTCTGACAGCAACAGCCGGCGGGTCTTTAAAATCAAGTCCACTGT	3960
GGTGGTGAAGGACCTTGTCAAGAACTCTGAGGTGGTTGCGGGGACAGGTGACCAGTGCCT	4020
CCCCTTTGATGACACTCGCTGCGGGGATGGTGGGAAGGCCACAGAAGCCACACTCACCAA	4080
TCCCAGGGGTATTACAGTGGACAAGTTTGGGCTGATCTACTTCGTGGATGGCACCATGAT	4140
CAGACGCATCGATCAGAATGGGATCATCTCCACCCTGCTCGGCTCTAATGATCTCACATC	4200
AGCCCGGCCACTCAGCTGTGATTCTGTCATGGATATTTCCCAGGTAAGACTGGAGTGGCC	4260
CACAGACTTAGCCATCAACCCAATGGACAACTCACTTTATGTCCTCGACAACAATGTGGT	4320
CCTGCAAATCTCTGAAAACCACCAGGTGCGCATTGTCGCCGGGAGGCCCATGCACTGCCA	4380
GGTCCCTGGCATTGACCACTTCCTGCTAAGCAAGGTGGCCATCCACGCAACCCTGGAGTC	4440
AGCCACCGCTTTGGCTGTTTCACACAATGGGGTCCTGTATATTGCTGAGACTGATGAGAA	4500
AAAGATCAACCGCATCAGGCAGGTCACCACTAGTGGAGAGATCTCACTCGTTGCTGGGGC	4560
CCCCAGTGGCTGTGACTGTAAAAATGATGCCAACTGTGATTGTTTTTCTGGAGACGATGG	4620
TTATGCCAAGGATGCAAAGTTAAATACCCCATCTTCCTTGGCTGTGTGTGCTGATGGGGA	4680
GCTCTACGTGGCCGACCTTGGGAACATCCGAATTCGGTTTATCCGGAAGAACAAGCCTTT	4740
CCTCAACACCCAGAACATGTATGAGCTGTCTTCACCAATTGACCAGGAGCTCTATCTGTT	4800
TGATACCACCGGCAAGCACCTGTACACCCAAAGCCTGCCCACAGGAGACTACCTGTACAA	4860
CTTCACCTACACTGGGGACGGCGACATCACACTCATCACAGACAACAATGGCAACATGGT	4920
AAATGTCCGCCGAGACTCTACTGGGATGCCCCTCTGGCTGGTGGTCCCAGATGGCCAGGT	4980
GTACTGGGTGACCATGGGCACCAACAGTGCACTCAAGAGTGTGACCACACAAGGACACGA	5040
GTTGGCCATGATGACATACCATGGCAATTCCGGCCTTCTGGCAACCAAAAGCAATGAAAA	5100
CGGATGGACAACATTTTATGAGTACGACAGCTTTGGCCGCCTGACAAATGTGACCTTCCC	5160
TACTGGCCAGGTGAGCAGTTTCCGAAGTGATACAGACAGTTCAGTGCATGTCCAGGTAGA	5220
GACCTCCAGCAAGGATGATGTCACCATAACCACCAACCTGTCTGCCTCAGGCGCCTTCTA	5280
CACACTGCTGCAAGACCAAGTCCGGAACAGCTACTACATCGGGGCCGATGGCTCCTTGCG	5340
GCTGCTGCTGGCCAACGGCATGGAGGTGGCGCTGCAGACTGAGCCCCACTTGCTGGCTGG	5400
CACCGTCAACCCCACCGTGGGCAAGAGGAATGTCACGCTGCCCATCGACAACGGCCTCAA	5460
CCTGGTGGAGTGGCGCCAGCGCAAAGAGCAGGCTCGGGGCCAGGTCACTGTCTTTGGGCG	5520
CCGGCTGCGGGTGCACAACCGAAATCTCCTATCTCTGGACTTTGATCGCGTAACACGCAC	5580
AGAGAAGATCTATGATGACCACCGCAAGTTCACCCTTCGGATTCTGTACGACCAGGCGGG	5640
GCGGCCCAGCCTCTGGTCACCCAGCAGCAGGCTGAATGGTGTCAACGTGACATACTCCCC	5700
TGGGGGTTACATTGCTGGCATCCAGAGGGGCATCATGTCTGAAAGAATGGAATACGACCA	5760
GGCGGGCCGCATCACATCCAGGATCTTCGCTGATGGGAAGACATGGAGCTACACATACTT	5820
AGAGAAGTCCATGGTGCTGCTACTACACAGCCAGAGGCAGTATATCTTTGAGTTCGACAA	5880
GAATGACCGCCTCTCTTCTGTGACGATGCCCAACGTGGCGCGGCAGACACTAGAGACCAT	5940
CCGCTCAGTGGGCTACTACAGAAACATCTATCAGCCCCCTGAGGGCAATGCCTCAGTCAT	6000
ACAGGACTTCACTGAGGATGGGCACCTCCTTCACACCTTCTACCTGGGCACTGGCCGCAG	6060
GGTGATATACAAGTATGGCAAACTGTCAAAGCTGGCAGAGACGCTCTATGACACCACCAA	6120
GGTCAGTTTCACCTATGACGAGACGGCAGGCATGCTGAAGACCATCAACCTACAGAATGA	6180
GGGCTTCACCTGCACCATCCGCTACCGTCAGATTGGGCCCCTGATTGACCGACAGATCTT	6240
CCGCTTCACTGAGGAAGGCATGGTCAACGCCCGTTTTGACTACAACTATGACAACAGCTT	6300

CCGGGTGACCAGCATGCAGGCTGTGATCAACGAGACCCCACTGCCCATTGATCTCTATCG	6360
CTATGATGATGTGTCAGGCAAGACAGAGCAGTTTGGGAAGTTTGGTGTCATTTACTATGA	6420
CATTAACCAGATCATCACCACAGCTGTCATGACCCACACCAAGCATTTTGATGCATATGG	6480
CAGGATGAAGGAAGTGCAGTATGAGATCTTCCGCTCGCTCATGTACTGGATGACCGTCCA	6540
GTATGATAACATGGGGCGAGTAGTGAAGAAGGAGCTGAAGGTAGGACCCTACGCCAATAC	6600
CACTCGCTACTCCTATGAGTATGATGCTGACGCCAGCTGCAGACAGTCTCCATCAATGA	6660
CAAGCCACTCTGGCGCTACAGCTACGACCTCAATGGGAACCTGCACTTACTGAGCCCTGG	6720
GAACAGTGCACGGCTCACACCACTACGGTATGACATCCGCGACCGCATCACTCGGCTGGG	6780
TGACGTGCAATACAAGATGGATGAGGATGGCTTCCTGAGGCAGCGGGGCGGTGATATCTT	6840
TGAGTACAACTCAGCTGGCCTGCTCATCAAGGCCTACAACCGGGCTGGCAGCTGGAGTGT	6900
CAGGTACCGCTACGATGGCCTGGGCGGCGCGTGTCCAGCAAGAGCAGCCACAGCCACCA	6960
CCTGACGTTCTTCTATGCAGACCTGACCCACCCACCAAGGTCACCCACCTGTACAACCA	7020
CTCCAGCTCTGAGATCACCTCCCTCTACTACGACTTGCAAGGACACCTCTTTGCCATGGA	7080
GCTGAGCAGTGGTGATGAGTTTTACATAGCTTGTGACAACATCGGGACCCCTCTTGCTGT	7140
CTTTAGTGGAACAGGTTTGATGATCAAGCAAATCCTGTACACAGCCTATGGGGAGATCTA	7200
CATGGATACCAACCCCAACTTTCAGATCATCATAGGCTACCATGGTGGCCTCTATGATCC	7260
ACTCACCAAGCTTGTCCACATGGGCCGGCGAGATTATGATGTGCTGGCCGGACGCTGGAC	7320
TAGCCCAGACCACGAGCTGTGGAAGCACCTTAGTAGCAGCAACGTCATGCCTTTTAATCT	7380
CTATATGTTCAAAAACAACAACCCCATCAGCAACTCCCAGGACATCAAGTGCTTCATGAC	7440
AGATGTTAACAGCTGGCTGCTCACCTTTGGATTCCAGCTACACAACGTGATCCCTGGTTA	7500
TCCCAAACCAGCATGGATGCCATGCAACCCTCCTACGAGCTCATCCACACACAGATGAA	7560
AACGCAGGAGTGGGACAACAGCAAGTCTATCCTCGGGGTACAGTGTGAAGTACAGAAGCA	7620
GCTCAAGGCCTTTGTCACCTTAGAACGGTTTGACCAGCTCTATGGCTCCACAATCACCAG	7680
CTGCCAGCAGGCTCCAAAGACCAAGAAGTTTGCATCCAGCGGCTCAGTCTTTGGCAAGGG	7740
GGTCAAGTTTGCCTTGAAGGATGGCCGAGTGACCACAGACATCATCAGTGTGGCCAATGA	7800
GGATGGGCGAAGGGTTGCTGCCATCTTGAACCATGCCCACTACCTAGAGAACCTGCACTT	7860
CACCATTGATGGGGTGGATACCCATTACTTTGTGAAACCAGGACCTTCAGAAGGTGACCT	7920
GGCCATCCTGGGCCTCAGTGGGGGGCGGCGAACCCTGGAGAATGGGGTCAACGTCACTGT	7980
GTCCCAGATCAACACAGTACTTAATGGCAGGACTAGACGCTACACAGACATCCAGCTCCA	8040
GTACGGGGCACTGTGCTTGAACACACGCTACGGGACAACGTTGGATGAGGAGAAGGCACG	8100
GGTCCTGGAGCTGGCCGGCAGAGAGCCGTGCGCCAAGCGTGGGCCCGCGAGCAGCAGAG	8160
ACTGCGGGAAGGGGAGGAAGGCCTGCGGGCCTGGACAGAGGGGGAGAAGCAGCAGGTGCT	8220
GAGCACAGGGCGGGTGCAAGGCTACGACGGCTTTTTCGTGATCTCTGTCGAGCAGTACCC	8280
AGAACTGTCAGACAGCGCCAACAACATCCACTTCATGAGACAGAGCTGAGATGGGCCGGAG	8340
GTGACAGAGAGGAC	

A disclosed NOV4 nucleic acid maps to chromosome 11, and is found in at least brain, spinal chord, testis, heart, lung, parathyroid, stomach, breast, colon, epidermis, ovary and kidney. A NOV4 nucleic acid has 7504 of 8359 bases (89%) identical to a gb:GENBANK-ID:AB025413|acc: AB025413.1 mRNA from Mus musculus TEN-M4.

A NOV4 polypeptide (SEQ ID NO:14) encoded by SEQ ID NO:13 is 2769 amino acid residues and is presented using the one letter code in Table 4B. Signal P, Psort and/or Hydropathy results predict that NOV4 does not have a signal peptide and is likely to be localized mitochondrial inner membrane with a certainty of 0.8363. In other embodiments, NOV4 may also be localized to the plasma membrane with a certainty of 0.65 or to the nucleus with a certainty of 0.6000, or microbody with a certainty of 0.3936.

Table 4B. NOV4 Polypeptide SEQ ID NO:14	
MDVKERKPYRSLTRRRDAERRYTSSSADSEEGKAPQKSYSSSETLKAYDQDARLAYGSRV	60
KDIVPQEAEEFCRTGANFTLRELGLEEVTPPHGTLYRTDIGLPQCGYSMGAGSDADMEAD	120
TVLSPEHPVRLWGRSTRSGRSSCLSSRANSNLTLTDTEHENTETDHPGGLQNHARLRTPP	180
PPLSHAHTPNQHHAASINSLNRGNFTPRSNPSPAPTDHSLSGEPPAGGAQEPAHAQENWL	240
LNSNIPLETRNLGKQPFLGTLQDNLIEMDILGASRHDGAYSDGHFLFKPGGTSPLFCTTS	300
PGYPLTSSTVYSPPPRPLPRSTFARPAFNLKKPSKYCNWKCAALSAIVISATLVILLAYF	360
VAMHLFGLNWHLQPMEGQMYEITEDTASSWPVPTDVSLYPSGGTGLETPDRKGKGTTEGK	420
PSSFFPEDSFIDSGEIDVGRRASQKIPPGTFWRSQVFIDHPVHLKFNVSLGKAALVGIYG	480
RKGLPPSHTQFDFVELLDGRRLLTQEARSLEGTPRQSRGTVPPSSHETGFIQYLDSGIWH	540
LAFYNDGKESEVVSFLTTAIESVDNCPSNCYGNGDCISGTCHCFLGFLGPDCGRASCPVL	600
CSGNGQYMKGRCLCHSGWKGAECDVPTNQCIDVACSNHGTCITGTCICNPGYKGESCEEV	660
DCMDPTCSGRGVCVRGECHCFVGWGGTNCETPRATCLDQCSGHGTFLPDTGLCSCDPSWT	720
GHDCSIEICAADCGGHGVCVGGTCRCEDGWMGAACDQRACHPRCAEHGTCRDGKCECSPG	780
WNGEHCTIAHYLDRVVKEGCPGLCNGNGRCTLDLNGWHCVCQLGWRGAGCDTSMETACGD	840
SKDNDGDGLVDCMDPDCCLQPLCHINPLCLGSPNPLDIIQETQVPVSQQNLHSFYDRIKF	900
LVGRDSTHIIPGENPFDGGHACVIRGQVMTSDGTPLVGVNISFVNNPLFGYTISRQDGSF	960
DLVTNGGISIIILRFERAPFITQEHTLWLPWDRFFVMETIIMRHEENEIPSCDLSNFARPN	1020
PVVSPSPLTSFASSCAEKGPIVPEIQALQEEISISGCKMRLSYLSSRTPGYKSVLRISLT	1080
HPTIPFNLMKVHLMVAVEGRLFRKWFAAAPDLSYYFIWDKTDVYNQKVFGLSEAFVSVGY	1140
EYESCPDLILWEKRTTVLQGYEIDASKLGGWSLDKHHALNIQSGILHKGNGENQFVSQQP	1200
PVIGSIMGNGRRRSISCPSCNGLADGNKLLAPVALTCGSDGSLYVGDFNYIRRIFPSGNV	1260
TNILELRNKDFRHSHSPAHKYYLATDPMSGAVFLSDSNSRRVFKIKSTVVVKDLVKNSEV	1320
VAGTGDQCLPFDDTRCGDGGKATEATLTNPRGITVDKFGLIYFVDGTMIRRIDQNGIIST	1380
LLGSNDLTSARPLSCDSVMDISQVRLEWPTDLAINPMDNSLYVLDNNVVLQISENHQVRI	1440
VAGRPMHCQVPGIDHFLLSKVAIHATLESATALAVSHNGVLYIAETDEKKINRIRQVTTS	1500
GEISLVAGAPSGCDCKNDANCDCFSGDDGYAKDAKLNTPSSLAVCADGELYVADLGNIRI	1560
RFIRKNKPFLNTQNMYELSSPIDQELYLFDTTGKHLYTQSLPTGDYLYNFTYTGDGDITL	1620
ITDNNGNMVNVRRDSTGMPLWLVVPDGQVYWVTMGTNSALKSVTTQGHELAMMTYHGNSG	1680
LLATKSNENGWTTFYEYDSFGRLTNVTFPTGQVSSFRSDTDSSVHVQVETSSKDDVTITT	1740
NLSASGAFYTLLQDQVRNSYYIGADGSLRLLLANGMEVALQTEPHLLAGTVNPTVGKRNV	1800
TLPIDNGLNLVEWRQRKEQARGQVTVFGRRLRVHNRNLLSLDFDRVTRTEKIYDDHRKFT	1860
LRILYDQAGRPSLWSPSSRLNGVNVTYSPGGYIAGIQRGIMSERMEYDQAGRITSRIFAD	1920
GKTWSYTYLEKSMVLLLHSQRQYIFEFDKNDRLSSVTMPNVARQTLETIRSVGYYRNIYQ	1980
PPEGNASVIQDFTEDGHLLHTFYLGTGRRVIYKYGKLSKLAETLYDTTKVSFTYDETAGM	2040
LKTINLQNEGFTCTIRYRQIGPLIDRQIFRFTEEGMVNARFDYNYDNSFRVTSMQAVINE	2100
TPLPIDLYRYDDVSGKTEQFGKFGVIYYDINQIITTAVMTHTKHFDAYGRMKEVQYEIFR	2160
SLMYWMTVQYDNMGRVVKKELKVGPYANTTRYSYEYDADGQLQTVSINDKPLWRYSYDLN	2220
GNLHLLSPGNSARLTPLRYDIRDRITRLGDVQYKMDEDGFLRQRGGDIFEYNSAGLLIKA	2280
YNRAGSWSVRYRYDGLGRRVSSKSSHSHHLQFFYADLTNPTKVTHLYNHSSSEITSLYYD	2340
LQGHLFAMELSSGDEFYIACDNIGTPLAVFSGTGLMIKQILYTAYGEIYMDTNPNFQIII	2400
GYHGGLYDPLTKLVHMGRRDYDVLAGRWTSPDHELWKHLSSSNVMPFNLYMFKNNNPISN	2460
SQDIKCFMTDVNSWLLTFGFQLHNVIPGYPKPDMDAMEPSYELIHTQMKTQEWDNSKSIL	2520
GVQCEVQKQLKAFVTLERFDQLYGSTITSCQQAPKTKKFASSGSVFGKGVKFALKDGRVT	2580
TDIISVANEDGRRVAAILNHAHYLENLHFTIDGVDTHYFVKPGPSEGDLAILGLSGGRRT	2640
LENGVNVTVSQINTVLNGRTRRYTDIQLQYGALCLNTRYGTTLDEEKARVLELARQRAVR	2700
QAWAREQQRLREGEEGLRAWTEGEKQQVLSTGRVQGYDGFFVISVEQYPELSDSANNIHF	2760
MRQSEMGRR	

The full amino acid sequence of the protein of the invention was found to have 2688 of 2771 amino acid residues (97%) identical to, and 2728 of 2771 amino acid residues (98%) similar to, the 2771 amino acid residue ptnr:SPTREMBL-ACC:Q9WTS7 protein from Mus musculus TEN-M4.

NOV4 also has homology to the amino acid sequences shown in the BLASTP data listed in Table 4C.

Table 4C. BLAST results for NOV4

Gene Index/ Identifier	Protein/ Organism	Length (aa)	Identity (%)	Positives (%)	Expect
gi|16551957|dbj|BAB 71206.1| (AK056531)	unnamed protein product [Homo sapiens]	730	99	99	0.0
gi|7657417|ref|NP 035987.2| (NM_011857)	odd Oz/ten-m homolog 3 (Drosophila); odd Oz/ten-m homolog 1 (Drosophila) [Mus musculus]	2715	66	79	0.0
gi|13649010|ref|X P 010128.3| XM_010128	odz (odd Oz/ten-m, Drosophila) homolog 1 [Homo sapiens]	2725	62	76	0.0
gi|1079143|pir||S 47008	tenascin-like protein - fruit fly (Drosophila melanogaster)	2515	33	53	0.0
gi|8922444|ref|NP 060574.1| (NM_018104)	hypothetical protein FLJ10474; hypothetical protein FLJ10886 [Homo sapiens]	1045	99	99	0.0

The homology of these sequences is shown graphically in the ClustalW analysis shown in Table 4D.

Table 4D ClustalW Analysis of NOV4

Tables 4E lists the domain description from DOMAIN analysis results against NOV4. This indicates that the NOV4 sequence has properties similar to those of other proteins known to contain this domain.

```
1) NOV4 (SEQ ID NO:13)
2) gi|16551957 (SEQ ID NO:50)
3) gi|7657417 (SEQ ID NO:51)
4) gi|13649010 (SEQ ID NO:52)
5) gi|1079143 (SEQ ID NO:53)
6) gi|8922444 (SEQ ID NO:54)
10        20        30        40        50
          ....|....|....|....|....|....|....|....|....|....|
NOV4      MDVKERKPTRSLT-RRRDAERRTTSSSADSKEGKAP-QKSYSSSETLKAY
gi|16551957|  --------------------------------------------------
gi|7657417|   MDVKSRRPYCSLTKSRRSKSRRTTNSGADWEECRVPTQKSYSSSETLKAP
gi|13649010|  MEQTDCKFYQPLPKVKHSMDLAYTSSSDSSDGRKP-RQSYNSRETLHSY
```

```
gi|1079143|    --------------------------------------------------
gi|8922444|    --------------------------------------------------

                        60        70        80        90       100
               ....|....|....|....|....|....|....|....|....|....|
NOV4           DQD-ARLAYGSRVKDIVPQEAEEFCRTGANFTLRELGLEEVTPPHGTLYR
gi|16551957|   --------------------------------------------------
gi|7657417|    DHDYSRLLYGNRVKDLVHREADEYTRQGQNFTLRQLGVCESATRRGVAFC
gi|13649010|   NQELR----------MN-YNSQSRKRKEVEKSTQEMEFCRTSHTLCSGYQ
gi|1079143|    -----------------------------------MNFRKDLVARCSSPW
gi|8922444|    --------------------------------------------------

                       110       120       130       140       150
               ....|....|....|....|....|....|....|....|....|....|
NOV4           TDLG-LPQCGYSLGAGSDADMEADTVLSPEHPVRLWGRSTRSGRSSCLSS
gi|16551957|   --------------------------------------------------
gi|7657417|    AEMG-LPHRGYSLSAGSDADTENEAVMSPEHAMRLWGRGVKSGRSSCLSS
gi|13649010|   TDMHSVSRHGYQLEMGSDVDTETEGAASPDHALRMWIRGMKSEHSSCLSS
gi|1079143|    PGSGSLSVLFAFLVMLILLTTTGVIKWNQSPPCSELVGNEASEVLTAKSA
gi|8922444|    --------------------------------------------------

                       160       170       180       190       200
               ....|....|....|....|....|....|....|....|....|....|
NOV4           RANSNLTLTDTEHENTETDH------------------------PGGLQN
gi|16551957|   --------------------------------------------------
gi|7657417|    RSNSALTLTDSEHENRSDSE------------------------SEQPSN
gi|13649010|   RANSALSLTDTDHERKSDGENGFKFSPVCCDMEAQAGSTQDVQSSPHNQF
gi|1079143|    NTDLSKLHNSSVRAKNGQGIG-------------------------LAQG
gi|8922444|    --------------------------------------------------

                       210       220       230       240       250
               ....|....|....|....|....|....|....|....|....|....|
NOV4           HARLRTPPPPLSHAHTPNQHHAASINSLNRGNFTPRSNPSPAPTDHSLSG
gi|16551957|   --------------------------------------------------
gi|7657417|    NPGQPTLQPLPPSHKQHPAQHHPSITSLNRNSLTNRRNQSPAPPAALPSE
gi|13649010|   TFRPLPPPPPPPHACTCARKPPPAADSLQRRSMTTRSQPSPAAPAPPTST
gi|1079143|    QSGLGAAGVGSGGGSSAATVTTATSNSGTAQGLQSTSASAESTSSAATSS
gi|8922444|    --------------------------------------------------

                       260       270       280       290       300
               ....|....|....|....|....|....|....|....|....|....|
NOV4           EPPAGGAQEPAHAQENWLLNSNIPLETRNLGKQPFLGTLQDNLIEMDILG
gi|16551957|   --------------------------------------------------
gi|7657417|    LQTTP---ESVQLQDSWVLGSNVPLESR----------------------
gi|13649010|   QDS-------VHLHNSWVLNSNIPLETR----------------------
gi|1079143|    SQS-----------------------------------------------
gi|8922444|    --------------------------------------------------

                       310       320       330       340       350
               ....|....|....|....|....|....|....|....|....|....|
NOV4           ASRHDGAYSDGHFLFKPGGTSPLFCTTSPGYPLTSSTVYSPPPRPLERSS
gi|16551957|   --------------------------------------------------
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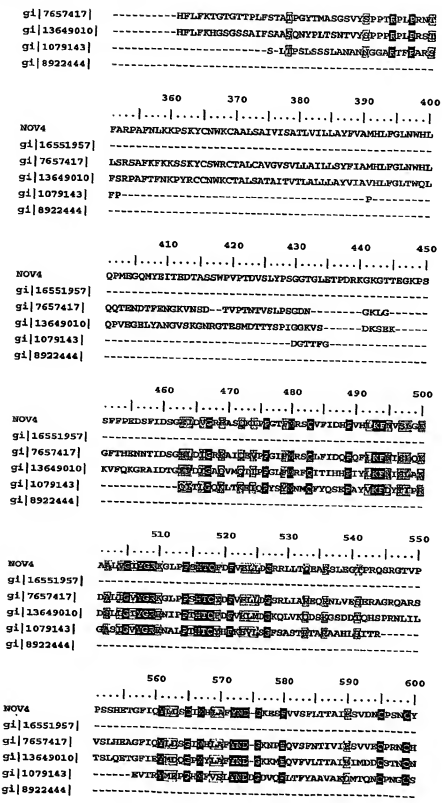
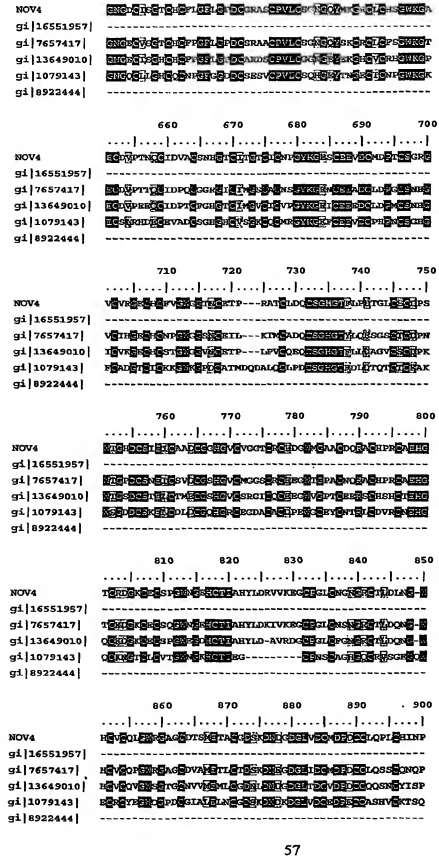


56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gi|7657417|
gi|13649010|
gi|1079143|
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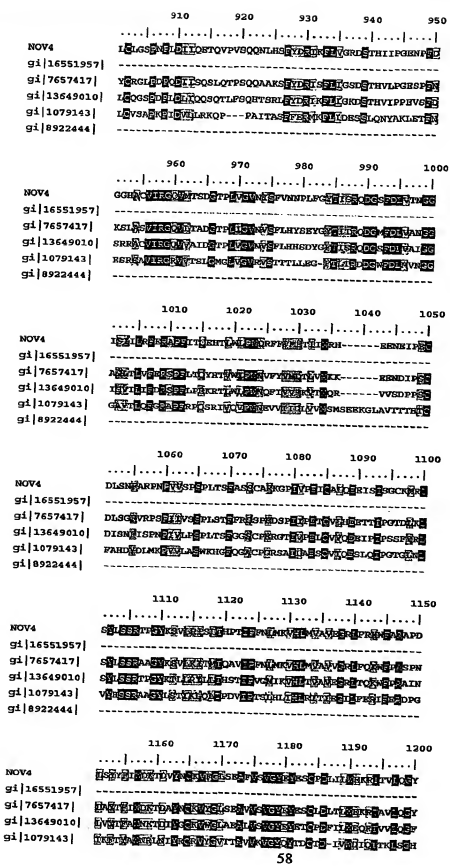
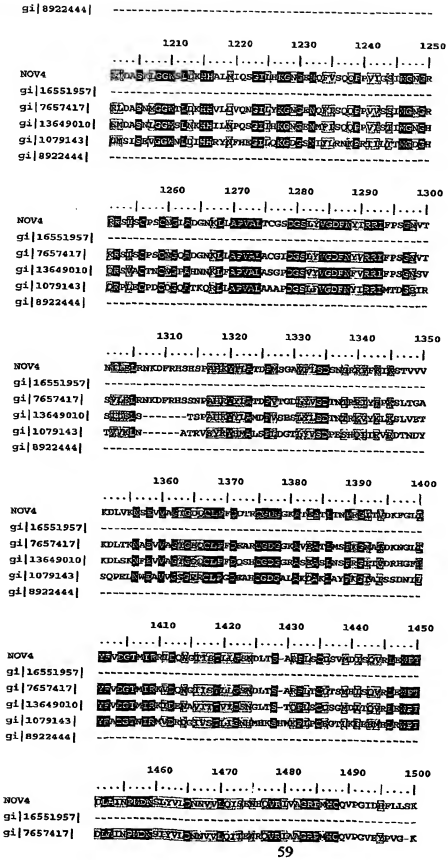
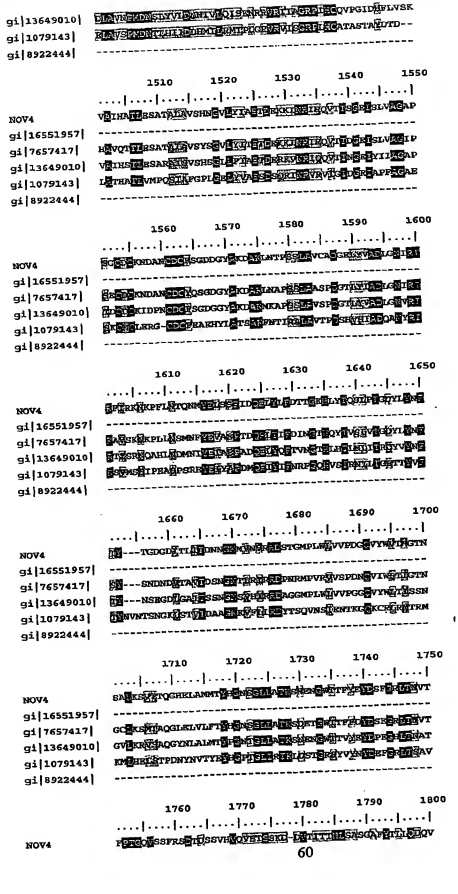
710 720 730 740 750
760 770 780 790 800
810 820 830 840 850
860 870 880 890 900


910 920 930 940 950
NOV4
gi|16551957|
gi|7657417|
gi|13649010|
gi|1079143|
gi|8922444|
960 970 980 990 1000
NOV4
gi|16551957|
gi|7657417|
gi|13649010|
gi|1079143|
gi|8922444|
1010 1020 1030 1040 1050
NOV4
gi|16551957|
gi|7657417|
gi|13649010|
gi|1079143|
gi|8922444|
1060 1070 1080 1090 1100
NOV4
gi|16551957|
gi|7657417|
gi|13649010|
gi|1079143|
gi|8922444|
1110 1120 1130 1140 1150
NOV4
gi|16551957|
gi|7657417|
gi|13649010|
gi|1079143|
gi|8922444|
1160 1170 1180 1190 1200
NOV4
gi|16551957|
gi|7657417|
gi|13649010|
gi|1079143|

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NOV4
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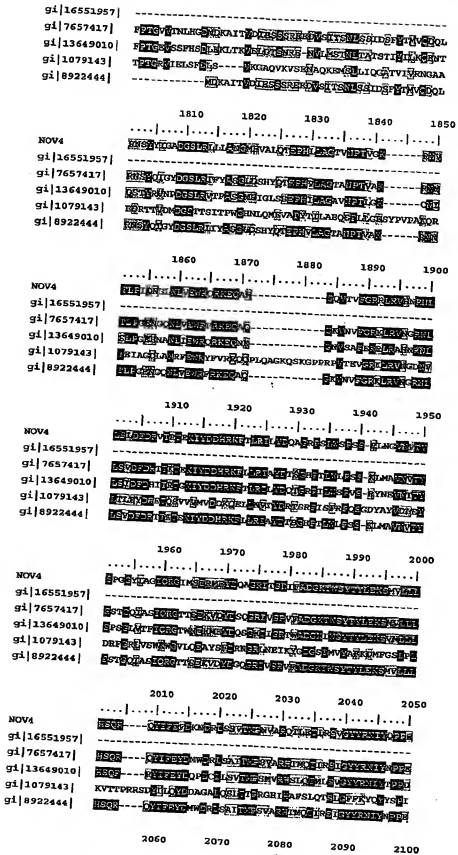
gi|1079143|
gi|8922444|
1560 1570 1580 1590 1600
NOV4
gi|16551957|
gi|7657417|
gi|13649010|
gi|1079143|
gi|8922444|
1610 1620 1630 1640 1650
NOV4
gi|16551957|
gi|7657417|
gi|13649010|
gi|1079143|
gi|8922444|
1660 1670 1680 1690 1700
NOV4
gi|16551957|
gi|7657417|
gi|13649010|
gi|1079143|
gi|8922444|
1710 1720 1730 1740 1750
NOV4
gi|16551957|
gi|7657417|
gi|13649010|
gi|1079143|
gi|8922444|
1760 1770 1780 1790 1800
NOV4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gi|13649010|
gi|1079143|
gi|8922444|
NOV4
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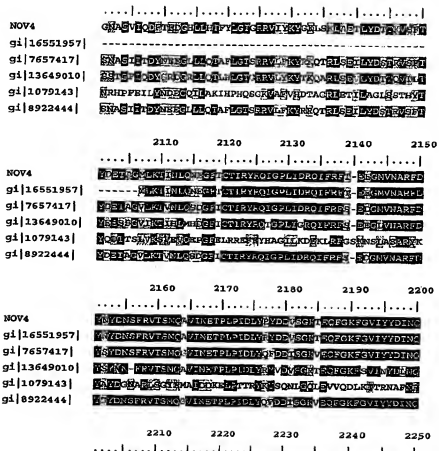
1860 1870 1880 1890 1900
1910 1920 1930 1940 1950
1960 1970 1980 1990 2000
2010 2020 2030 2040 2050
2060 2070 2080 2090 2100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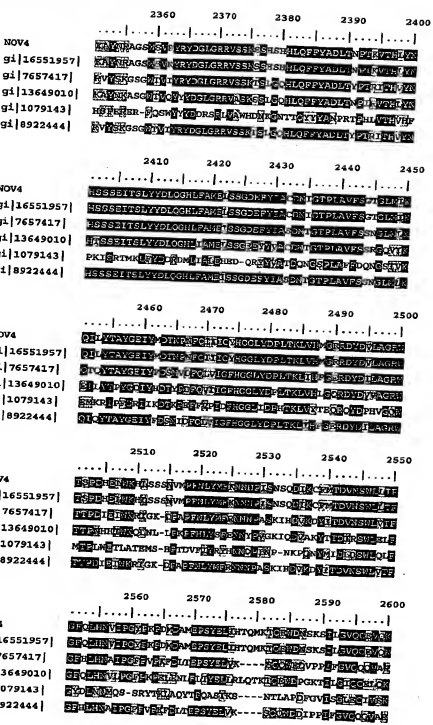
gi|1079143|
gi|8922444|
2110 2120 2130 2140 2150
2160 2170 2180 2190 2200
2210 2220 2230 2240 2250
2260 2270 2280 2290 2300
2310 2320 2330 2340 2350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2560 2570 2580 2590 2600
2610 2620 2630 2640 2650
NOV4
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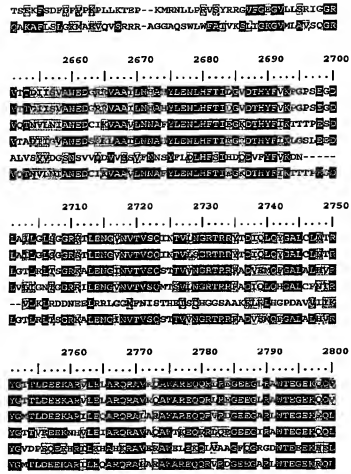
gi|7657417|
gi|13649010|
gi|1079143|
gi|8922444|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gi|8922444|
2660 2670 2680 2690 2700
NOV4
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gi|7657417|
gi|13649010|
gi|1079143|
gi|8922444|
2710 2720 2730 2740 2750
NOV4
gi|16551957|
gi|7657417|
gi|13649010|
gi|1079143|
gi|8922444|
2760 2770 2780 2790 2800
NOV4
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gi|13649010|
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gi|8922444|
2810 2820 2830 2840 2850
NOV4
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gi|7657417|
gi|13649010|
gi|1079143|
gi|8922444|
2860
NOV4
gi|16551957|
gi|7657417|
gi|13649010|
gi|1079143|
gi|8922444|

Table 4E. Domain Analysis of NOV4

gnl|Pfam|pfam01500, Keratin_B2, Keratin, high sulfur B2 protein. High sulfur proteins are cysteine-rich proteins synthesized during the differentiation of hair matrix cells, and form hair fibers in association with hair keratin intermediate filaments. This family has been divided up into four regions, with the second region containing 8 copies of a short repeat. This family is also known as B2 or KAP1.

CD-Length = 144 residues, 87.5% aligned
Score = 38.9 bits (89), Expect = 0.004

```
Query:  630  CIDVACSNHGTCITGTCICNPGYKGSSCEEVDCMDPTCSGRGVCVRGECHCFVGWGGTNC
689

             C    CS  GTC +  C      +  SC +  C  P CS    C R  C          + C
Sbjct:  5    CGFPTCSTLGTCGSSCC------QPPSCCQPSCCQPVCSQTTCC-RPTCFQSSCCRPSCC
57

Query:  690  ETP--RATCLDQCSGHGTFLPDTGLCSCDPSWTGHDCSIEICAADCGGHGVCVGGTCRCE
747

             +T   + TC    S         G+ SC   W   DC +E
Sbjct:  58   QTSCCQPTCCQSSSCQ----TGCGIGSCRTRWCRPDCRVE--------------------
93

Query:  748  DGWMGAACDQRACHPRCAEHGTCRDGKCECS---PGWNGEHC   786
                   C    C    C+    + S   P + G+ C
Sbjct:  94   -----GTCLPPCCVVSCTPPTCCQPVSAQASCCRPSYCGQSC   130
```

The novel TEN-M-like protein encoded by the gene of invention has highest homology to the mouse TEN-M4 protein, which belongs to the ODZ/TENM family of proteins. This family was first identified in Drosophila as being a pair-rule gene affecting segmentation of the early embryo. It was the first pair-rule gene identified that was not a transcription factor, but a type II transmembrane protein. Vertebrate homologs of the TENM family have been identified in mouse and zebrafish. In the mouse, TEN-M4 expression was found to be on the cell surface, in the brain, trachea as well as developing limb and bone. Analysis of the TEN-M1 protein reveals that it can bind to itself, making it likely that TEN-M4 may be a dimeric moiety as well. In cell culture experiments, fragments of the TEN-M proteins can bind the Drosophila PS2 integrins. In addition, members of the TEN-M family have been identified to be downstream of the endoplasmic reticulum stress response pathway, which alters the response of cells to their environment. This suggests that the ODZ/TENM family may be involved in cell adhesion, spreading and motility. Translocations leading to the fusion of this gene with the NRG1/HGL gene from chromosome 8 have been found to generate a paracrine growth factor for one mammary carcinoma cell line, termed gamma-heregulin. Therefore this novel gene may have widespread implications in development, regeneration and carcinogenesis of various tissues.

Two new potential ligands of the Drosophila PS2 integrins have been characterized by functional interaction in cell culture. These potential ligands are a new Drosophila laminin alpha2 chain encoded by the wing blister locus and Ten-m, an extracellular protein known to be involved in embryonic pattern formation. As with previously identified PS2 ligands, both contain RGD sequences, and RGD-containing fragments of these two proteins (DLAM-RGD and TENM-RGD) can support PS2 integrin-mediated cell spreading. In all cases, this spreading is inhibited specifically by short RGD-containing peptides. As previously found for the PS2 ligand tiggrin (and the tiggrin fragment TIG-RGD), TENM-RGD induces maximal spreading of cells expressing integrin containing the alphaPS2C splice variant. This is in contrast to DLAM-RGD, which is the first Drosophila polypeptide shown to interact preferentially with cells expressing the alphaPS2 m8 splice variant. The betaPS integrin subunit also varies in the presumed ligand binding region as a result of alternative splicing. For TIG-RGD and TENM-RGD, the beta splice variant has little effect, but for DLAM-RGD, maximal cell spreading is supported only by the betaPS4A form of the protein. Thus, the diversity in PS2 integrins due to splicing variations, in combination with diversity of matrix ligands, can greatly enhance the functional complexity of PS2-ligand interactions in the developing animal. The data also suggest that the splice variants may alter regions of the subunits that are directly involved in ligand interactions, and this is discussed with respect to models of integrin structure.

A sequence of about thirty to forty amino-acid residues long found in the sequence of epidermal growth factor (EGF) has been shown to be present, in a more or less conserved form, in a large number of other, mostly animal proteins. The list of proteins currently known to contain one or more copies of an EGF-like pattern is large and varied. The functional significance of EGF domains in what appear to be unrelated proteins is not yet clear. However, a common feature is that these repeats are found in the extracellular domain of membrane-bound proteins or in proteins known to be secreted (exception: prostaglandin G/H synthase). The EGF domain includes six cysteine residues which have been shown (in EGF) to be involved in disulfide bonds. The main structure is a two-stranded beta-sheet followed by a loop to a C-terminal short two-stranded sheet. Subdomains between the conserved cysteines vary in length. The NHL (NCL-1, HT2A and LIN-41) repeat is found in a variety of enzymes of the copper type II, ascorbate-dependent monooxygenase family which catalyse the C-terminus alpha-amidation of biological peptides. The repeat also occurs in a human zinc finger protein that specifically interacts with the activation domain of lentiviral Tat proteins. The repeat domain that is often associated with RING finger and B-box motifs (see, Ben-Zur T,

Dev Biol 2000 Jan 1;217(1):107-20; Adelaide J, Int J Oncol 2000 Apr;16(4):683-8 ; Wang XZ, Oncogene 1999 Oct 7;18(41):5718-21; Schaefer G, Oncogene 1997 Sep 18;15(12):1385-94 ; Wang XZ, EMBO J 1998 Jul 1;17(13):3619-30; Baumgartner S, EMBO J 1994 Aug 15;13(16):3728-40; Otaki JM, Dev Biol 1999 Aug 1;212(1):165-81; Mieda M, Mech Dev 1999 Sep;87(1-2):223-7; Oohashi T, J Cell Biol 1999 May 3;145(3):563-77; Graner MW, J Biol Chem 1998 Jul 17;273(29):18235-41, incorporated herein by reference).

The protein similarity information, expression pattern, and map location for the TEN-M4-like protein and nucleic acid disclosed herein suggest that this TEN-M4-like protein may have important structural and/or physiological functions characteristic of this family. Therefore, the nucleic acids and proteins of the invention are useful in potential diagnostic and therapeutic applications and as a research tool. These include serving as a specific or selective nucleic acid or protein diagnostic and/or prognostic marker, wherein the presence or amount of the nucleic acid or the protein are to be assessed, as well as potential therapeutic applications such as the following: (i) a protein therapeutic, (ii) a small molecule drug target, (iii) an antibody target (therapeutic, diagnostic, drug targeting/cytotoxic antibody), (iv) a nucleic acid useful in gene therapy (gene delivery/gene ablation), and (v) a composition promoting tissue regeneration *in vitro* and *in vivo* (vi) biological defense weapon.

The NOV4 nucleic acids and proteins of the invention are useful in potential diagnostic and therapeutic applications implicated in various diseases and disorders described below and/or other pathologies. For example, the compositions of the present invention will have efficacy for treatment of patients suffering from: cardiac diseases, myocardial contractility in failing heart and other diseases, disorders and conditions of the like. The disclosed NOV4 nucleic acid of the invention encoding a TEN-M4-like protein includes the nucleic acid whose sequence is provided in Table 4A or a fragment thereof. The invention also includes a mutant or variant nucleic acid any of whose bases may be changed from the corresponding base shown in Table 4A while still encoding a protein that maintains TEN-M4-like protein-like activities and physiological functions, or a fragment of such a nucleic acid. The invention further includes nucleic acids whose sequences are complementary to those just described, including nucleic acid fragments that are complementary to any of the nucleic acids just described. The invention additionally includes nucleic acids or nucleic acid fragments, or complements thereto, whose structures include chemical modifications. Such modifications include, by way of nonlimiting example, modified bases, and nucleic acids whose sugar phosphate backbones are modified or derivatized. These modifications are carried out at least in part to enhance the chemical stability of the modified nucleic acid, such that they may be

used, for example, as antisense binding nucleic acids in therapeutic applications in a subject. In the mutant or variant nucleic acids, and their complements, up to about 11 percent of the bases may be so changed.

The disclosed NOV4 protein of the invention includes the TEN-M4-like protein whose sequence is provided in Table 3B. The invention also includes a mutant or variant protein any of whose residues may be changed from the corresponding residue shown in Table 4B while still encoding a protein that maintains beta adrenergic receptor kinase-like activities and physiological functions, or a functional fragment thereof. In the mutant or variant protein, up to about 3 percent of the residues may be so changed.

The protein similarity information, expression pattern, and map location for TEN-M4-like protein and nucleic acid (NOV4) disclosed herein suggest that NOV4 may have important structural and/or physiological functions characteristic of the TEN-M4 protein family. Therefore, the NOV4 nucleic acids and proteins of the invention are useful in potential diagnostic and therapeutic applications. These include serving as a specific or selective nucleic acid or protein diagnostic and/or prognostic marker, wherein the presence or amount of the nucleic acid or the protein are to be assessed, as well as potential therapeutic applications such as the following: (i) a protein therapeutic, (ii) a small molecule drug target, (iii) an antibody target (therapeutic, diagnostic, drug targeting/cytotoxic antibody), (iv) a nucleic acid useful in gene therapy (gene delivery/gene ablation), and (v) a composition promoting tissue regeneration *in vitro* and *in vivo*.

The NOV4 nucleic acids and proteins of the invention are useful in potential diagnostic and therapeutic applications implicated in various diseases and disorders described below. For example, the compositions of the present invention will have efficacy for treatment of patients suffering from: Von Hippel-Lindau (VHL) syndrome, Alzheimer's disease, stroke, tuberous sclerosis, hypocalcaemia, Parkinson's disease, Huntington's disease, cerebral palsy, epilepsy, Lesch-Nyhan syndrome, multiple sclerosis, ataxia-telangiectasia, leukodystrophies, behavioral disorders, addiction, anxiety, pain, neurodegeneration, fertility disorders, hyperparathyroidism, hypoparathyroidism, cardiomyopathy, atherosclerosis, hypertension, congenital heart defects, aortic stenosis, atrial septal defect (ASD), atrioventricular (A-V) canal defect, ductus arteriosus, pulmonary stenosis, subaortic stenosis, ventricular septal defect (VSD), valve diseases, tuberous sclerosis, scleroderma, obesity, transplantation disorders, diabetes, autoimmune disease, renal artery stenosis, interstitial nephritis, glomerulonephritis, polycystic kidney disease, systemic lupus erythematosus, renal tubular acidosis, IgA nephropathy, hypocalcaemia, asthma, emphysema, scleroderma, allergy, ARDS, Hirschsprung's disease,

WHAT IS CLAIMED IS:

1. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:
   (a) a mature form of an amino acid sequence selected from the group consisting of SEQ ID NOS:2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, and 34;
   (b) a variant of a mature form of an amino acid sequence selected from the group consisting of SEQ ID NOS:2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, and 34, wherein one or more amino acid residues in said variant differs from the amino acid sequence of said mature form, provided that said variant differs in no more than 15% of the amino acid residues from the amino acid sequence of said mature form;
   (c) an amino acid sequence selected from the group consisting SEQ ID NOS:2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, and 34; and
   (d) a variant of an amino acid sequence selected from the group consisting of SEQ ID NOS:2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, and 34, wherein one or more amino acid residues in said variant differs from the amino acid sequence of said mature form, provided that said variant differs in no more than 15% of amino acid residues from said amino acid sequence.

2 The polypeptide of claim 1, wherein said polypeptide comprises the amino acid sequence of a naturally-occurring allelic variant of an amino acid sequence selected from the group consisting SEQ ID NOS:2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, and 34.

3. The polypeptide of claim 2, wherein said allelic variant comprises an amino acid sequence that is the translation of a nucleic acid sequence differing by a single nucleotide from a nucleic acid sequence selected from the group consisting of SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, and 35.

4. The polypeptide of claim 1, wherein the amino acid sequence of said variant comprises a conservative amino acid substitution.

5. An isolated nucleic acid molecule comprising a nucleic acid sequence encoding a polypeptide comprising an amino acid sequence selected from the group consisting of:

(a) a mature form of an amino acid sequence selected from the group consisting of SEQ ID NOS:2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, and 34;

(b) a variant of a mature form of an amino acid sequence selected from the group consisting of SEQ ID NOS:2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, and 34, wherein one or more amino acid residues in said variant differs from the amino acid sequence of said mature form, provided that said variant differs in no more than 15% of the amino acid residues from the amino acid sequence of said mature form;

(c) an amino acid sequence selected from the group consisting of SEQ ID NOS:2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, and 34;

(d) a variant of an amino acid sequence selected from the group consisting SEQ ID NOS:2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, and 34, wherein one or more amino acid residues in said variant differs from the amino acid sequence of said mature form, provided that said variant differs in no more than 15% of amino acid residues from said amino acid sequence;

(e) a nucleic acid fragment encoding at least a portion of a polypeptide comprising an amino acid sequence chosen from the group consisting of SEQ ID NOS:2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, and 34, or a variant of said polypeptide, wherein one or more amino acid residues in said variant differs from the amino acid sequence of said mature form, provided that said variant differs in no more than 15% of amino acid residues from said amino acid sequence; and

(f) a nucleic acid molecule comprising the complement of (a), (b), (c), (d) or (e).

6. The nucleic acid molecule of claim 5, wherein the nucleic acid molecule comprises the nucleotide sequence of a naturally-occurring allelic nucleic acid variant.

7. The nucleic acid molecule of claim 5, wherein the nucleic acid molecule encodes a polypeptide comprising the amino acid sequence of a naturally-occurring polypeptide variant.

8. The nucleic acid molecule of claim 5, wherein the nucleic acid molecule differs by a single nucleotide from a nucleic acid sequence selected from the group consisting of SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, and 35.

9. The nucleic acid molecule of claim 5, wherein said nucleic acid molecule comprises a nucleotide sequence selected from the group consisting of:
   (a) a nucleotide sequence selected from the group consisting of SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, and 35;
   (b) a nucleotide sequence differing by one or more nucleotides from a nucleotide sequence selected from the group consisting of SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, and 35, provided that no more than 20% of the nucleotides differ from said nucleotide sequence;
   (c) a nucleic acid fragment of (a); and
   (d) a nucleic acid fragment of (b).

10. The nucleic acid molecule of claim 5, wherein said nucleic acid molecule hybridizes under stringent conditions to a nucleotide sequence chosen from the group consisting SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, and 35, or a complement of said nucleotide sequence.

11. The nucleic acid molecule of claim 5, wherein the nucleic acid molecule comprises a nucleotide sequence selected from the group consisting of:
   (a) a first nucleotide sequence comprising a coding sequence differing by one or more nucleotide sequences from a coding sequence encoding said amino acid sequence, provided that no more than 20% of the nucleotides in the coding sequence in said first nucleotide sequence differ from said coding sequence;
   (b) an isolated second polynucleotide that is a complement of the first polynucleotide; and
   (c) a nucleic acid fragment of (a) or (b).

12. A vector comprising the nucleic acid molecule of claim 11.

13. The vector of claim 12, further comprising a promoter operably-linked to said nucleic acid molecule.

14. A cell comprising the vector of claim 12.

15. An antibody that binds immunospecifically to the polypeptide of claim 1.

16. The antibody of claim 15, wherein said antibody is a monoclonal antibody.

17. The antibody of claim 15, wherein the antibody is a humanized antibody.

18. A method for determining the presence or amount of the polypeptide of claim 1 in a sample, the method comprising:
(a) providing the sample;
(b) contacting the sample with an antibody that binds immunospecifically to the polypeptide; and
(c) determining the presence or amount of antibody bound to said polypeptide,
thereby determining the presence or amount of polypeptide in said sample.

19. A method for determining the presence or amount of the nucleic acid molecule of claim 5 in a sample, the method comprising:
(a) providing the sample;
(b) contacting the sample with a probe that binds to said nucleic acid molecule; and
(c) determining the presence or amount of the probe bound to said nucleic acid molecule,
thereby determining the presence or amount of the nucleic acid molecule in said sample.

20. The method of claim 19 wherein presence or amount of the nucleic acid molecule is used as a marker for cell or tissue type.

21. The method of claim 20 wherein the cell or tissue type is cancerous.

22. A method of identifying an agent that binds to a polypeptide of claim 1, the method comprising:
(a) contacting said polypeptide with said agent; and
(b) determining whether said agent binds to said polypeptide.

23. The method of claim 22 wherein the agent is a cellular receptor or a downstream effector.

24. A method for identifying an agent that modulates the expression or activity of the polypeptide of claim 1, the method comprising:
(a) providing a cell expressing said polypeptide;
(b) contacting the cell with said agent, and
(c) determining whether the agent modulates expression or activity of said polypeptide,
whereby an alteration in expression or activity of said peptide indicates said agent modulates expression or activity of said polypeptide.

25. A method for modulating the activity of the polypeptide of claim 1, the method comprising contacting a cell sample expressing the polypeptide of said claim with a compound that binds to said polypeptide in an amount sufficient to modulate the activity of the polypeptide.

26. A method of treating or preventing a NOVX-associated disorder, said method comprising administering to a subject in which such treatment or prevention is desired the polypeptide of claim 1 in an amount sufficient to treat or prevent said NOVX-associated disorder in said subject.

27. The method of claim 26 wherein the disorder is selected from the group consisting of cardiomyopathy and atherosclerosis.

28. The method of claim 26 wherein the disorder is related to cell signal processing and metabolic pathway modulation.

29. The method of claim 26, wherein said subject is a human.

30. A method of treating or preventing a NOVX-associated disorder, said method comprising administering to a subject in which such treatment or prevention is desired

the nucleic acid of claim 5 in an amount sufficient to treat or prevent said NOVX-associated disorder in said subject.

31. The method of claim 30 wherein the disorder is selected from the group consisting of cardiomyopathy and atherosclerosis.

32. The method of claim 30 wherein the disorder is related to cell signal processing and metabolic pathway modulation.

33. The method of claim 30, wherein said subject is a human.

34. A method of treating or preventing a NOVX-associated disorder, said method comprising administering to a subject in which such treatment or prevention is desired the antibody of claim 15 in an amount sufficient to treat or prevent said NOVX-associated disorder in said subject.

35. The method of claim 34 wherein the disorder is diabetes.

36. The method of claim 34 wherein the disorder is related to cell signal processing and metabolic pathway modulation.

37. The method of claim 34, wherein the subject is a human.

38. A pharmaceutical composition comprising the polypeptide of claim 1 and a pharmaceutically-acceptable carrier.

39. A pharmaceutical composition comprising the nucleic acid molecule of claim 5 and a pharmaceutically-acceptable carrier.

40. A pharmaceutical composition comprising the antibody of claim 15 and a pharmaceutically-acceptable carrier.

41. A kit comprising in one or more containers, the pharmaceutical composition of claim 38.

42. A kit comprising in one or more containers, the pharmaceutical composition of claim 39.

43. A kit comprising in one or more containers, the pharmaceutical composition of claim 40.

44. A method for determining the presence of or predisposition to a disease associated with altered levels of the polypeptide of claim 1 in a first mammalian subject, the method comprising:

(a) measuring the level of expression of the polypeptide in a sample from the first mammalian subject; and

(b) comparing the amount of said polypeptide in the sample of step (a) to the amount of the polypeptide present in a control sample from a second mammalian subject known not to have, or not to be predisposed to, said disease;

wherein an alteration in the expression level of the polypeptide in the first subject as compared to the control sample indicates the presence of or predisposition to said disease.

45. The method of claim 44 wherein the predisposition is to a cancer.

46. A method for determining the presence of or predisposition to a disease associated with altered levels of the nucleic acid molecule of claim 5 in a first mammalian subject, the method comprising:

(a) measuring the amount of the nucleic acid in a sample from the first mammalian subject; and

(b) comparing the amount of said nucleic acid in the sample of step (a) to the amount of the nucleic acid present in a control sample from a second mammalian subject known not to have or not be predisposed to, the disease;

wherein an alteration in the level of the nucleic acid in the first subject as compared to the control sample indicates the presence of or predisposition to the disease.

47. The method of claim 46 wherein the predisposition is to a cancer.

48. A method of treating a pathological state in a mammal, the method comprising administering to the mammal a polypeptide in an amount that is sufficient to alleviate the pathological state, wherein the polypeptide is a polypeptide having an amino acid sequence at least 95% identical to a polypeptide comprising an amino acid sequence of at least one of SEQ ID NOS:2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, and 34, or a biologically active fragment thereof.

49. A method of treating a pathological state in a mammal, the method comprising administering to the mammal the antibody of claim 15 in an amount sufficient to alleviate the pathological state.